

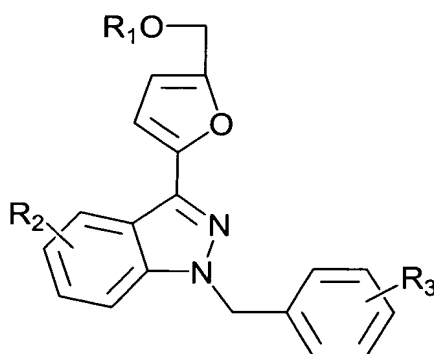
## **WHAT IS CLAIMED IS:**

1. A method of inhibiting HIF-1 $\alpha$  expression in tumor cells or tissues, comprising contacting the tumor cells or tissues with a composition comprising 3-(5'-hydroxymethyl-2'-furyl)-1-benzylindazole at an effective amount for inhibiting HIF-1 $\alpha$  expression, wherein said tumor is selected from the group consisting of hepatoma, stomach carcinoma, renal carcinoma, cervical carcinoma, neuroblastoma, and prostate carcinoma.
2. A method of inhibiting HIF-1-regulated gene expression in tumor cells or tissues, comprising contacting the tumor cells or tissues with a composition comprising 3-(5'-hydroxymethyl-2'-furyl)-1-benzylindazole at an effective amount for inhibiting HIF-1-regulated gene expression, wherein said tumor is selected from the group consisting of hepatoma, stomach carcinoma, renal carcinoma, cervical carcinoma, neuroblastoma, and prostate carcinoma.
3. A method of inhibiting angiogenesis in tumor cells or tissues, comprising contacting the tumor cells or tissues with a composition comprising 3-(5'-hydroxymethyl-2'-furyl)-1-benzylindazole at an effective amount for inhibiting angiogenesis, wherein said tumor is selected from the group consisting of hepatoma, stomach carcinoma, renal carcinoma, cervical carcinoma, neuroblastoma and prostate carcinoma.
4. A method of inhibiting tumor growth in animal tissues, comprising contacting the tumor cells or tissues with a composition comprising 3-(5'-hydroxymethyl-2'-furyl)-1-benzylindazole at an effective amount for inhibiting tumor growth, wherein said tumor is selected from the group consisting of hepatoma, stomach carcinoma, renal carcinoma, cervical carcinoma, neuroblastoma, and prostate carcinoma.
5. A method of inhibiting tumor progression and metastasis in animal tissues, comprising contacting the tumor cells or tissues with a composition comprising 3-(5'-hydroxymethyl-2'-furyl)-1-benzylindazole at an effective amount for inhibiting tumor

progression and metastasis, wherein said tumor is selected from the group consisting of hepatoma, stomach carcinoma, renal carcinoma, cervical carcinoma, neuroblastoma, and prostate carcinoma.

6. A method of treating a HIF-1-mediated disorder or condition in a mammal comprising administering to the mammal a composition comprising a therapeutically effective amount of 3-(5'-hydroxymethyl-2'-furyl)-1-benzylindazole, wherein said HIF-1-mediated disorder or condition is selected from the group consisting of hepatoma, stomach carcinoma, renal carcinoma, cervical carcinoma, neuroblastoma, and prostate carcinoma.

7. A method of inhibiting HIF-1 $\alpha$  expression in tumor cells or tissues, comprising contacting the tumor cells or tissues with a composition comprising a compound or mixture of compounds of the Formula I at an effective amount for inhibiting HIF-1 $\alpha$  expression:



wherein:

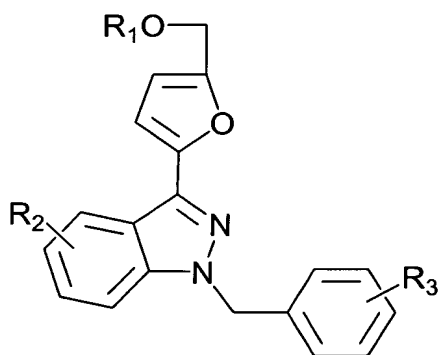
R<sub>1</sub> is a polyol; and

R<sub>2</sub> and R<sub>3</sub> are independently chosen from hydrogen, optionally substituted alkyl, optionally substituted alkoxy, halogen, nitro, substituted amino, alkylsulfonyl, alkylsulfanyl, aminocarbonyl, alkoxy carbonyl, optionally substituted aryl and optionally substituted heteroaryl;

including single isomers, mixtures of isomers, and pharmaceutically acceptable solvates and salts thereof.

8. The method of claim 7, wherein said tumor is selected from the group consisting of hepatoma, stomach carcinoma, renal carcinoma, cervical carcinoma and neuroblastoma, and prostate carcinoma.

9. A method of inhibiting HIF-1-regulated gene expression in tumor cells or tissues, comprising contacting the tumor cells or tissues with a composition comprising a compound or mixture of compounds of the Formula I at an effective amount for inhibiting HIF-1-regulated gene expression:



wherein:

R<sub>1</sub> is a polyol; and

R<sub>2</sub> and R<sub>3</sub> are independently chosen from hydrogen, optionally substituted alkyl, optionally substituted alkoxy, halogen, nitro, substituted amino, alkylsulfonyl, alkylsulfanyl, aminocarbonyl, alkoxy carbonyl, optionally substituted aryl and optionally substituted heteroaryl;

including single isomers, mixtures of isomers, and pharmaceutically acceptable solvates and salts thereof.

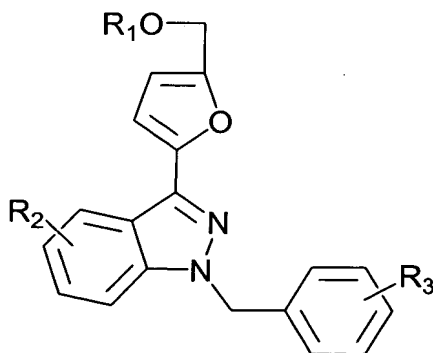
10. The method of claim 9 wherein said HIF-1-regulated gene is selected from the group consisting of erythropoietin, transferrin, transferrin receptor, ceruloplasmin, vascular endothelial growth factor (VEGF), VEGF receptor FLT-1, transforming growth factor  $\beta$ 3, plasminogen activator inhibitor 1,  $\alpha$ 1B adrenergic receptor, adrenomedullin, endothelin 1, nitric oxide synthase 2, heme oxygenase 1, glucose transporter 1 and 3, hexokinase 1 and 2, enolase 1, glyceraldehyde-3-phosphate dehydrogenase,

phosphoglycerate kinase 1, phosphoglucokinase L, pyruvate kinase M, aldolase A and C, rios phosphate isomerase, lactate dehydrogenase A, carbonic anhydrase 9, adenylate kinase 3, propyl-4-hydroxylase a1, insulin-like growth factor (IGF) 2, IGP-binding protein 1, 2 and 3, P21, Nip3, cyclin G2 and differentiated embryo chondrocyte 1.

11. The method of claim 10, wherein said HIF-1-regulated gene is selected from the group consisting of VEGF, aldolase A and enolase 1.

12. The method of claim 9, wherein said tumor is selected from the group consisting of hepatoma, stomach carcinoma, renal carcinoma, cervical carcinoma, neuroblastoma, and prostate carcinoma.

13. A method of inhibiting angiogenesis in tumor cells or tissues, comprising contacting the tumor cells or tissues with a composition comprising a compound or mixture of compounds of the Formula I at an effective amount for inhibiting angiogenesis:



wherein:

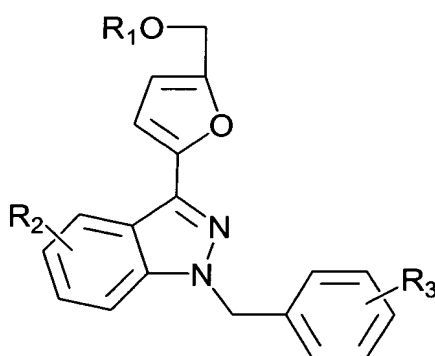
R<sub>1</sub> is a polyol; and

R<sub>2</sub> and R<sub>3</sub> are independently chosen from hydrogen, optionally substituted alkyl, optionally substituted alkoxy, halogen, nitro, substituted amino, alkylsulfonyl, alkylsulfanyl, aminocarbonyl, alkoxycarbonyl, optionally substituted aryl and optionally substituted heteroaryl;

including single isomers, mixtures of isomers, and pharmaceutically acceptable solvates and salts thereof.

14. The method of claim 13, wherein said tumor is selected from the group consisting of hepatoma, stomach carcinoma, renal carcinoma, cervical carcinoma, neuroblastoma, and prostate carcinoma.

15 A method of inhibiting tumor growth in animal tissues, comprising contacting the tumor cells or tissues with a composition comprising a compound or mixture of compounds of the Formula I at an effective amount for inhibiting tumor growth:



wherein:

R<sub>1</sub> is a polyol; and

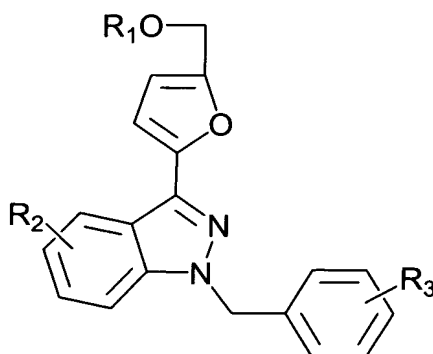
R<sub>2</sub> and R<sub>3</sub> are independently chosen from hydrogen, optionally substituted alkyl, optionally substituted alkoxy, halogen, nitro, substituted amino, alkylsulfonyl, alkylsulfanyl, aminocarbonyl, alkoxy carbonyl, optionally substituted aryl and optionally substituted heteroaryl;

including single isomers, mixtures of isomers, and pharmaceutically acceptable solvates and salts thereof.

16. The method of claim 15, wherein said tumor is selected from the group consisting of hepatoma, stomach carcinoma, renal carcinoma, cervical carcinoma, neuroblastoma, and prostate carcinoma.

17. A method of inhibiting tumor progression and metastasis in animal tissues, comprising contacting the tumor cells or tissues with a composition comprising a

compound or a mixture of compounds of the Formula I at an effective amount for inhibiting tumor progression and metastasis:



wherein:

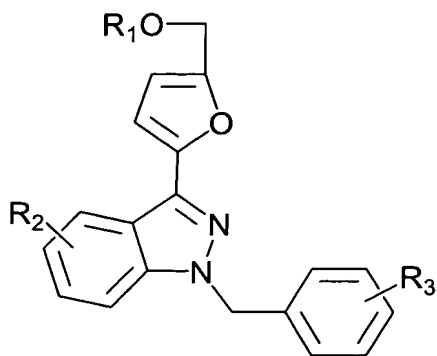
$R_1$  is a polyol; and

$R_2$  and  $R_3$  are independently chosen from hydrogen, optionally substituted alkyl, optionally substituted alkoxy, halogen, nitro, substituted amino, alkylsulfonyl, alkylsulfanyl, aminocarbonyl, alkoxy carbonyl, optionally substituted aryl and optionally substituted heteroaryl;

including single isomers, mixtures of isomers, and pharmaceutically acceptable solvates and salts thereof.

18. The method of claim 17, wherein said tumor is selected from the group consisting of hepatoma, stomach carcinoma, renal carcinoma, cervical carcinoma, neuroblastoma, and prostate carcinoma.

19. A method of treating a HIF-1-mediated disorder or condition in a mammal comprising administering to the mammal a composition comprising a therapeutically effective amount of a compound or a mixture of compounds of the Formula I:



wherein:

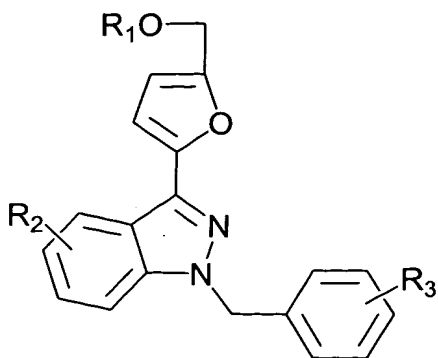
R<sub>1</sub> is a polyol; and

R<sub>2</sub> and R<sub>3</sub> are independently chosen from hydrogen, optionally substituted alkyl, optionally substituted alkoxy, halogen, nitro, substituted amino, alkylsulfonyl, alkylsulfanyl, aminocarbonyl, alkoxy carbonyl, optionally substituted aryl and optionally substituted heteroaryl;

including single isomers, mixtures of isomers, and pharmaceutically acceptable solvates and salts thereof.

20. The method of claim 19, wherein said HIF-1-mediated disorder or condition is selected from the group consisting of hepatoma, stomach carcinoma, renal carcinoma, cervical carcinoma, neuroblastoma, and prostate carcinoma.

21. A pharmaceutical composition comprising an amount effective of a compound or mixture of compounds of the Formula I to inhibit tumor angiogenesis, tumor growth or tumor progression and metastasis in a host in need thereof, or to treat an HIF-1-mediated disorder or condition in a mammal; and a pharmaceutically acceptable carrier:



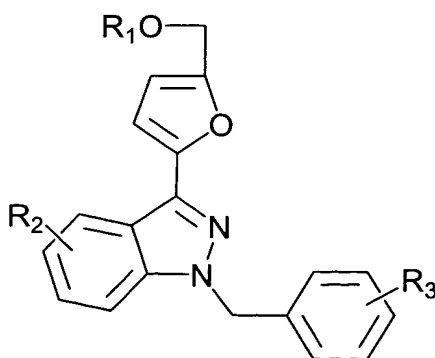
wherein:

R<sub>1</sub> is a polyol; and

R<sub>2</sub> and R<sub>3</sub> are independently chosen from hydrogen, optionally substituted alkyl, optionally substituted alkoxy, halogen, nitro, substituted amino, alkylsulfonyl, alkylsulfanyl, aminocarbonyl, alkoxycarbonyl, optionally substituted aryl and optionally substituted heteroaryl;

including single isomers, mixtures of isomers, and pharmaceutically acceptable solvates and salts thereof.

22. A compound of the Formula I:



wherein:

R<sub>1</sub> is a polyol; and

R<sub>2</sub> and R<sub>3</sub> are independently chosen from hydrogen, optionally substituted alkyl, optionally substituted alkoxy, halogen, nitro, substituted amino, alkylsulfonyl, alkylsulfanyl, aminocarbonyl, alkoxycarbonyl, optionally substituted aryl and optionally substituted heteroaryl;



including single isomers, mixtures of isomers, and pharmaceutically acceptable solvates and salts thereof.

23. A compound according to claim 22 wherein  $R_2$  and  $R_3$  are hydrogen.
24. A compound according to claim 22 wherein  $R_1$  is a 2-hydroxymethyl-pyran-3,4,5-triol-6-yl.
25. A compound according to claim 24 wherein  $R_2$  and  $R_3$  are hydrogen.